

Applicant : Paul D. Coleman *et al.*
Serial No. : 09/770,534
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Attorney's Docket No.: 12610-003002

REMARKS

Claims 57-100 are now pending in the application (claims 6-56 were cancelled by the preliminary amendment filed with the application and claims 1-5 are cancelled by present amendment). The present amendment adds new claims 57-100, which are supported by the specification and original claims, as described below. No new matter has been added.

New **claims 57 and 76** cover methods for creating a gene profile for a given stage of Alzheimer's disease by examining mRNA and protein expression, respectively. These claims are supported by original claim 1 and by the specification at, for example, page 18, lines 25-30, page 22, line 5 *et seq* (where Applicants describe conditions suitable for *in situ* hybridization and immunochemistry studies), and page 35, lines 1-9. The passage on page 35 begins (emphasis added): “[t]he present invention *focuses* on the examination of message *in single neurons* as opposed to proteins for a variety of reasons.” The reason given is that messages are localized to the cell body, but a number of proteins are transported to the axons, dendrites, and synapses that form between neurons at the ends of these projections. Accordingly, it can be difficult to say that a particular neuron (*e.g.*, one with frank neurofibrillary tangles) expresses a particular protein. Thus, while the invention may focus on message expression in the context of single neurons (and we note this is the focus, not the limit, of the invention, even in that context), the clear implication of the passage at page 35 is that, when *non-neural tissues* (as now claimed) are examined, protein expression can be analyzed.

New **claims 87 and 93** cover methods for determining whether an individual has Alzheimer's disease (claims 87 and 93 refer to claims 57 and 76, which are described above). New claims 87 and 93 are supported by original claim 1, and by the specification at, for example, page 18, lines 25-30, page 22, line 5 *et seq*, page 35, lines 1-9, and page 32, lines 30-31 (where Applicants specify that, in one embodiment, one of the cells examined is diseased (*e.g.*, affected by Alzheimer's disease) and one is healthy (as the cells obtained from the individual in claims 87 and 93 may be). New **claims 87 and 93** are also supported by the Examples; see especially Fig. 3 in which cells were obtained from three patients with Alzheimer's disease and two without.

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New **claims 99 and 100** cover methods for determining whether a compound affects the gene profile for a given stage of Alzheimer's disease. These claims are supported by original claims 16 and 34 and by the specification at, for example, page 32, lines 32-33.

New **claim 58**, which requires production and amplification of antisense RNA transcripts, is supported by original claim 16 and by the specification at, for example, Fig. 1 (which is a schematic presentation of the single cell approach to mRNA profiling).

New **claim 59** limits the way in which antisense RNA transcripts are quantitated, and is supported by original claims 8-10 and by the specification at, for example, page 21, line 28 through page 22, line 2. New **claims 73-75, 85-86, 90-92, and 96-98** limit the types of tissue or bodily fluids that are employed. These tissues and fluids are disclosed in the specification at, for example, page 27, lines 8-10 (see also original claim 14).

New **claims 60-64 and 77-81** limit the way in which Alzheimer's disease is staged. These claims are supported by the specification at, for example, page 5, lines 3-21, page 8, lines 29-32, and page 23, lines 7-25.

New **claims 65-72 and 88-89** specify a protein encoded by the mRNA. Similarly, new **claims 82-84 and 94-95** specify the protein *per se*. These claims are supported by original claim 7 and by the specification at, for example, page 28, line 30 through page 32, line 15 (see the discussion above regarding analysis of gene expression by examination of protein expression).

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The application is now in condition for examination, which action is respectfully requested. Enclosed is a check for \$117 for the claims fee. If there are any other charges, or any credits, please apply them to Deposit Account No. 06-1050.

Respectfully submitted,



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